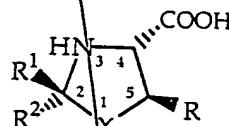


Claims

5 1. A cyclosporin derivative in which the peptide chain comprises at least one residue of a non-natural amino acid of general formula I:



(I)

10 in which

X denotes an oxygen or a sulfur;

R denotes a hydrogen, or an alkyl group having between 1 and 6 carbon atoms;

15 15 R₁ and R₂ denote, independently of each other, a hydrogen, an alkyl group, having between 1 and 6 carbons, which may be straight-chain or branched-chain, substituted or non-substituted, an alkylene group having between 1 and 6 carbon atoms, a substituted or non-substituted aryl group, a substituted or non-substituted heteroaryl group, a residue of a
20 water-soluble polymer, possibly bound to a spacer group.

2. The derivative according to Claim 1, characterized in that, in the amino acid of general formula I, R denotes a hydrogen or a methyl group.

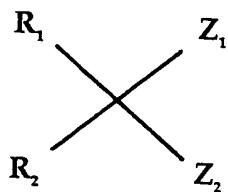
25 3. The derivative according to any of the preceding Claims, characterized in that it is derived from a cyclosporin in which the peptide chain contains at least one amino acid, chosen from serine, threonine and Sistine, in d or l configuration.

30 4. The derivative according to Claim 3, characterized in that at least one of the amino acids serine, threonine or Sistine of the basic cyclosporin is replaced by the amino acid of general formula I.

5. A method of preparation of the derivatives as in Claim 4, comprising an N,O-acetalisation reaction of at least one of the three amino acids serine, threonine and cysteine, by reacting the basic cyclosporin with a compound of formula II:

5

10



(II)

in which

Z_1 and Z_2 denote, independently of each other, a halogen, a hydroxyl group, an alkoxy group, or a thiol; or

15 both Z_1 and Z_2 together represent an oxygen of a carbonyl group or a sulfur of a thione; and

R_1 and R_2 are defined as above.

*add
a²*